

HIV VACCINE INDUSTRY THINK TANK

Hosted by the Global HIV Vaccine Enterprise
September 23, 2014

Purpose. The *HIV Vaccine Industry Think Tank* convened leaders from the public and private sectors actively involved in vaccine development to discuss and reevaluate the strategies and interfaces between the private and public sectors for developing an effective HIV vaccine.

Objectives. The aim of this meeting was to understand current dynamics and uncover strategies that will disrupt the status quo by helping all stakeholders position themselves advantageously within the HIV vaccine development ecosystem and optimize contributions to vaccine development in a way that upholds a commitment to public health objectives and public funding. The meeting also sought to identify opportunities to create a platform that would enable industry partners to play a more significant, end-to-end role in advancing HIV vaccine research and development.

A. Background and State of the Field

HIV vaccine development can benefit from more effective collaboration across sectors

A cooperative approach is essential to the HIV vaccine development process; no company or funder can develop an HIV vaccine in isolation. Although partners necessarily have different roles, needs and drivers, close collaboration among scientists, industry, government and funders along the discovery, development and delivery pathway is essential. As such, the collaborative potential of HIV vaccine development will be optimized when all stakeholders have a common understanding of the underlying guiding principles and their distinct roles and responsibilities.

Cross-Sector Collaboration – Guiding Principles

- We share a common goal
- We have complementary expertise and assets
- We operate with distinct priorities, incentives and constraints
- We often work independently and may have an incomplete appreciation of each other's commitment, capabilities and limitations
- We should think about finding ways to maximize our collective potential and compensate for our individual constraints

Enabling cross-sector collaboration through an end-to-end approach

Recognizing that HIV vaccine development could be accelerated by a clear, efficient and more predictable model for proactive and strategic cross-sector collaborations, the HIV Vaccine Industry Think Tank oriented participants to two guiding questions:

1. **How can industry be more involved in HIV vaccine research and development?**
2. **Is there a better way to conceptualize and implement a cross-sector collaborative model to execute an “end-to-end” process that develops and delivers an effective HIV vaccine as expeditiously as possible?**

Engaging industry more fully, and earlier, was recognized as a critical starting point in the development of a more collaborative, end-to-end approach to HIV vaccine development. Accordingly, there is a need to establish a common understanding of the private sector drivers of decision-making:

- Alternative development approaches are compared and assessed in order to identify the most promising strategy for achieving a desired goal.
- It is better to terminate a program early than have it fail later in development; high standards of program performance/success are set early and not lowered.
- Prioritization of projects/programs across portfolios is an unforgiving process, particularly in a highly resource-constrained environment.
- Ultimately, a sufficiently high probability of success (POS) is typically required to justify resource allocation and initiate a concerted development effort. Formally assessing the POS of a product/investment (i.e. scientific, regulatory criteria/desired label, manufacturing, favorable policy recommendation, IP access, implementation feasibility, potential demand, etc.) is conducted in a highly objective manner. This question in particular makes end-to-end development subject to market and profitability questions.

In addition to understanding and engaging with the drivers of decision-making within industry, the private sector currently implements a powerful and coherent “end-to-end” approach to its own product/vaccine development activities that could inform the refinement of a more collaborative, multisector partnership model for HIV vaccine development. Key tenets of the end-to-end product development approach include: i) **articulating a clear and compelling target product profile (TPP)** (e.g. target population, minimum efficacy level, safety/tolerability expectations, vaccine delivery route, dose/dosing schedule/fit with other vaccines, cost/feasibility/predictability of production approach, etc.) as a central organizing concept; ii) **defining a shared vision of the program strategy** that aligns teams from discovery to development to manufacturing to delivery; and iii) **setting and adhering to an overall plan for product development** early on, and offering minimal, if any, opportunities for modification as the program proceeds.

B. Building a Common Understanding of Development Challenges

Recognizing that defining an effective model that integrates all sectors from “end-to-end” presupposes a shared appreciation of challenges faced by each sector, representatives shared their differing perspectives on the distinct barriers and constraints delaying HIV vaccine development for their sector, and identified opportunities for strengthening engagement with industry. Commentary addressed five key themes.

1. Discovery Science Challenges. Developing an HIV vaccine has raised challenging immunological questions that have not previously been addressed or resolved in the development of other vaccines. Many believe that iterative, small-scale human studies (also called experimental medicine trials) designed to answer immunological questions that advance and enhance understanding of vaccine and viral immunology are required to inform the POS for true “end product” development. These experimental medicine trials aim to support immunogen discovery and/or development of novel immunization strategies, to inform and drive a classical product development pathway. Experimental medicine trials focus on discovery and the science of vaccines, without assuming a potential product development path. Initiating experimental medicine studies has been slow, due to high cost and time required to make multiple small-scale product lots of GMP-quality material in an iterative manner. Those costs can paralyze academic centers, particularly when resources or experience to manage CMOs

are also limited. Further, industry – although very well equipped to support manufacturing for this purpose – does not typically have the capacity or incentives in place to develop clinical candidates that are not potentially on the path to becoming an “end product”.

2. Preclinical and Clinical Development Challenges. Support for moving HIV vaccine concepts into proof of concept (efficacy) studies is encumbered by several limitations and considerations: i) once a product development path has started, that product cannot be changed substantially; ii) the absence of a correlate of protection and a predictive animal model present significant hurdles to early de-risking and therefore to achieving corporate commitment to product development; iii) decision-making around which idea/product to advance is competitive and multifactorial. Further, once initiated, efficacy studies necessitate large, long complicated trials. HIV vaccine development complexity is also amplified by the need to test vaccine efficacy against multiple/all clades or modes of transmission, all of which necessitate the development of a clear and compelling TPP. In addition, vaccine candidates proven safe and immunogenic might benefit from mechanisms to gather additional trend data that might support decision-making to move to an efficacy trial.

3. People/Talent Challenges. The pool of bioprocessing, technical operations, quality assurance and regulatory talent are all essential to the critical path but current resources aren’t sufficient to meet needs. Assigning these limited human resources to high-risk programs is, consequently, another barrier.

4. Financial/Resource Challenges. For-profit companies must be ever more results-oriented in their internal investments as they are of paramount priority to a company’s viability. As a result, internal resource allocation is fiercely competitive and product portfolio decisions are dependent on clear articulation of a convincing business case relative to other alternatives. Nevertheless, meeting participants acknowledged that mitigating circumstances, such as recognition of public good or corporate contribution to society can factor into resource decisions, particularly if success is likely or if there are powerful champions from a company’s board or most senior management.

5. Partnership Challenges. The transition from research to development is ambiguous, with the rules of engagement with industry much less clear on the research/discovery end. Accordingly, as multiple partners and sectors are increasingly and necessarily engaged in HIV vaccine product development, effective collaboration models with full and true alignment will be challenging to define. Specifically, it will be critical to align expectations of different contributors on the outcomes of a development path, and dedicate the time and resources necessary for negotiating successful bilateral agreements for collaborating and sharing information.

C. Industry’s Role: Break-out Sessions and Group Reporting

Break-out groups were asked to discuss four key questions, listed below. The groups arrived at similar conclusions, which indicated a collective understanding of the current situation, difficulties and challenges.

1. What are industry’s strengths and capabilities as a collaborator?

Industry has a powerful product and process development focus. Specifically, industry is well-positioned to bring: proven R&D capabilities; a mindset that infuses a product development perspective into decision-making while engaging in an end-to-end development process; established knowledge of how to work with, use and oversee CMOs; and project management excellence.

2. What are industry's limitations in HIV product development collaborations?

Given uncertainties of success of current vaccine candidates and a limited business case, there has not yet been enough success in this arena for major financial investment in HIV vaccine development from industry. In short, HIV product development initiatives will inevitably compete for resources in large corporations as industry primarily prioritizes other business-oriented programs.

3. What can industry address?

Industry is clearly well-positioned to lead advanced product development after proof-of-concept is achieved, but there may also be an opportunity for industry to engage partners pre-competitively by providing expertise, information or education in the following three areas:

PARTNERSHIP	PROCESS	PRODUCT DEVELOPMENT
<ul style="list-style-type: none"> Defining collaborative arrangements Selecting and vetting CMOs/CROs; sharing knowledge of how to work with CMO/CROs 	<ul style="list-style-type: none"> Advising on CMC, process development, and regulatory approaches (i.e. how to get product to clinic rapidly) Educating the field on PD and product scale-up Critical role in defining TPPs 	<ul style="list-style-type: none"> Access to reagents (e.g. adjuvants) on a specific basis Expertise in production (e.g. antibodies); often done in the spirit of shared value Advice on the development of animal models

4. How can other sectors position themselves?

Break-out groups focused on the pivotal role for funders and CMOs, which might be better positioned to support multisector product development partnerships. Specifically, **funders** were called upon to experiment with innovative financing incentives and non-traditional ownership structures in product development partnerships (e.g. captive asset vs. not-for-profit). Finally, work is underway by the Gates Foundation, IAVI and NIH toward establishing specialized - even dedicated - **CMOs** wherein HIV vaccine-specific expertise and capabilities to make complex proteins (particularly HIV env) can be located, developed and retained.

D. Partnerships and Collaboration

Invited speakers described a number of different product development partnerships for diverse diseases and product types that offered approaches, which could be considered and adapted, as we seek to refine and evolve collaboration in HIV vaccine development. Comparison of the practices, procedures and approaches of these partnerships points to several common success factors and best practices.

Approach to Partnership. Effective partnerships were secured by clear agreements set early in the partnership and grounded in a well-defined approach to governance, including decision-making mechanisms, clearly articulated roles and responsibilities and transparency in communication and data sharing.

Approach to Working with Private Sector. Committed Industry/Pharma partners were sought that were willing to provide sustainable investment at risk, such as early commitment to manufacturing. Notably, these partnerships generally assigned private sector players equal status with other partners.

Approach to Managing Risk. Recognizing the risk of product development in a complex partnership setting, effective partnerships established product development plans that shared risks and adhered to financial sustainability plans.

Approach to Product Development. Product development succeeded within partnerships that prepared a clear TPP that would allow multiple partners to de-risk work with novel technologies/approaches of mutual interest.

The partnerships examined, however, had varying objectives and some distinguishing approaches:

PATH Principles for Private-Sector Collaboration. PATH seeks to structure partnerships that advance technologies, strengthen systems and encourage healthy behaviors. Partnerships are grounded in a mutual appreciation for the contributions of all partners and a common **commitment to global access** inclusive of product supply, affordability and IP management.

The RTS,S Malaria Partnership. RTS,S is a vaccine development partnership established between GSK and PATH MVI, with significant funding from the Gates Foundation. RTS,S is focused on malaria control in infants and young children in malaria-endemic regions of Sub-Saharan Africa.

Vaccine Discovery Partnership (VxDP). VxDP provides an efficient mechanism for the Gates Foundation to directly engage Pharma to de-risk cross-cutting technologies of mutual interest. Notably, VxDP achieves its objectives by establishing an internal Gates Foundation **opportunity fund for innovative projects** and requiring Pharma partners to co-fund collaborative projects. As such, the VxDP mechanism facilitates, coordinate and integrate Pharma with the work of PDPs, biotech and academia to advance vaccine R&D across disease areas of mutual interest.

Innovative Medicines Initiative – 2 (IMI2). In response to a mandate to better exploit the potential of technology and entrepreneurship in healthcare, the European Union has placed greater emphasis on the creation of public private partnerships (P3s) such as IMI, now IMI-2, a joint undertaking between the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA) aiming to accelerate the development of better and safer medicines, including vaccines, for patients. IMI supports collaborative research projects and builds networks of industrial and academic experts. By **simplifying funding and reporting, investments target medium-sized industrial partners, academia, patient organizations and regulatory agencies.**

MSD-Wellcome Trust Hilleman Laboratories. A partnership between Merck and the Wellcome Trust was launched in 2009 to create a sustainable, not-for-profit Centre of Excellence to turn innovative science into practical solutions for those in greatest need. This partnership marks the **first time a research charity and a pharmaceutical company have partnered** to form a separate joint venture with equally shared funding and decision-making rights.

Small Biotech Perspective: GeoVax. GeoVax is focused on forging partnerships and attracting funding to support clade B HIV vaccine development. Their aim is to advance a vaccine through the proof-of-concept stage and out-license it to large pharma. Recognizing the challenges of securing investment in HIV vaccine development, **public funding remains vital to development plans of small biotechs, like GeoVax.**

TB Drug Accelerator (TBDA). The TBDA was established to improve on antiquated, first-line TB therapies by accelerating the development of shorter, safer TB drug regimens. TBDA focuses on discovery and preclinical development, conducting large-scale screening and progressing to lead optimization. TBDA's approach to partnership emphasizes early collaboration to minimize redundancy and **removes competitive barriers by enabling companies to work on each other's compounds.**

E. Advancing Key Issues: Primary Recommendations for Follow-up

Collectively, Think Tank participants have recognized the possibility of redefining the status quo in HIV vaccine development to better leverage industry, particularly during the vaccine discovery stage. To do so, however, there is a need to identify a partnership model among not-for-profit, academia and industry that adheres to the end-to-end model more closely.

A number of ways by which industry could improve the status quo of HIV vaccine development were raised during the course of the Think Tank:

- Industry has expertise in scanning early vaccine development programs for products with development potential; there is an opportunity to better define how this industry capability can be leveraged to support prioritization of new vaccine products/concepts and accelerate the transition from discovery to development.
- There is an opportunity to fine-tune the assays used to evaluate preclinical products in order to characterize a product structurally, and align a scientifically clear question with the right assays, equipment and experimentation to answer it.
- Explore and develop mechanisms to provide access to product components from industry (e.g. adjuvants) and support the ability to conduct head-to-head studies as well as investigations of correlates.
- Industry (in collaboration with CMOs) could provide greater support, expertise and/or oversight of chemistry, manufacturing and control (CMC) and vector development, particularly in terms of rapid manufacturing of small-scale clinical lots for discovery programs.
- HIV vaccine translational programs could benefit from an integrated, industry-quality project management approach.
- Industry could spearhead a consensus-building process among industry players focused on defining key measures of POS (NHP studies, experimental medicine studies, etc.) providing criteria to guide earlier interest and engagement of researchers with industry.
- While fostering greater investment from the private sector will always demand a persuasive and evidence based case, inclusive of a strong POS and return on investment, there is a need to articulate and defend other dimensions of value such as IP, know-how, social responsibility, market access, and trade-offs such as patent extension or guaranteed market or pricing.

What might encourage greater Big Pharma engagement?

With a view to encouraging greater engagement from the private sector, two interlinked strategies were proposed. First, we were invited to consider a model for early development wherein companies could work together in the pre-competitive space where private sector, academia, government collaborators are encouraged to partner on the development of standards, data or processes that are common across an industry and where adoption or use will advance the entire field. Industry participation in HIV vaccine development could serve them as a place to allow regulatory experts, CMC leads, clinicians, etc. to test/prove a technology platform, manufacturing process or analytic technology that is relevant for other portfolio programs.

While ambitious in vision and scope, consensus was built around a number of realistic first steps that would address the immediate need to accelerate, reduce the cost and optimize the productivity of experimental medicine studies:

1. **Explore Cross-Sector Internship Program.** Formalize the process of embedding industry in academia/not-for-profit and vice versa in the context of an internship or sabbatical program. An example of this is the joint agreement signed by the Industry (EFPIA) and EDCTP for the establishment of a **Fellowship scheme for Clinical Researchers in European-based pharmaceutical companies' research centres, among a few others.**
2. **Knowledge Sharing.** Explore and develop mutually beneficial ways that allow industry expertise to be shared more efficiently and effectively thereby preventing wasted time and resources in candidate development and early testing.
3. **Support CMC Production Requirements of Experimental Medicine Studies.** Academic stakeholders called for the development of augmented capabilities in CMC dedicated to supporting the HIV vaccine production requirements of experimental medicine studies. Two models, one existing and one novel were suggested and discussed:
 - **Center of Excellence in CMC.** The Gates Foundation/IAVI and NIH have begun development of a center of excellence in CMC; the center is at the planning stage with significant effort ahead. This center would consist of structural expertise and an analytics core.
 - **Expert Pool of Consultants.** Recognizing that extra capacity for a center of excellence in CMC is scarce in industry today, consider engaging recently retired individuals who are active as consultants in these specialties in the development of a supported, non-profit consulting pool or group.
4. **Accessing Industry Resources to Pilot Manufacturing Needs of the Field.** There is a willingness among at least a few industry representatives to initiate discussions among companies, funders and government agencies to determine how the field, including the private sector, might invest in the development of accessible pilot-scale manufacturing capabilities. A key challenge will be creating a persuasive and sustainable business case in the context of fluctuating demand and funding.

Recommendations and ideas that came up during the meeting clearly range in complexity, commitment and cost. Think Tank participants were supportive of these approaches to strengthen HIV vaccine development in principle. In practice, i) establishing an internship program to support cross-sector engagement represents a widely supported and achievable objective in the near-term; more ambitious, but also widely supported were: ii) assembling and mobilizing a pool of CMC-focused consultants; and iii) supporting virtual structures to enable knowledge sharing among HIV vaccine developers in all sectors.

There was a clear interest among industry scientists attending the Think Tank to advance those initiatives, but the field must recognize that this enthusiasm is tempered by the necessary and challenging requirement to obtain corporate/institutional support of these proposals. The Enterprise could be well-positioned to catalyze the necessary discussions among individuals and companies. Enabling change will be complex and difficult, necessitating active involvement of players from across all sectors and a shared commitment to advancing dialogue within their organizations. The POS of those initiatives remain to be determined.

By championing greater integration of industry capabilities in early development and testing of HIV vaccine products and concepts, there is an opportunity to accelerate product development in not only HIV, but also other priority disease areas.

Appendix A: Agenda

8:30-8:45 **Welcome Remarks and Meeting Objectives** – N. Russell, Enterprise Board Chair
Purpose and charge for meeting – B. Snow

8:45-10:45 **Background and State of the Field** – M. Feinberg moderates
Presentation: Companies' roles in HIV vaccine development thus far – J. Esparza
Viewpoint: End-to-end thinking and approach – M. Feinberg
Challenges Roundtable – discussants, 15 min per topic

- Research: B. Haynes and J. Mascola
- Pre-clinical Development: T. Hassell and S. Barnett
- Private Sector: J. Gerberding and J. Sadoff
- Funding: C. Dieffenbach and N. Russell

10:45-11:15 **Break**

11:15-12:00 **Industry's Role** – J. Tartaglia and A. Khan

Break-out groups: Break-out groups address strengths, roles and recommendations, bringing their thoughts to the full group for consolidation and prioritization

- Industry strengths, capabilities and limitations
- Challenges industry could help address
- How can other sectors best position themselves to engage with industry

12:00-12:15 **Pick up lunch**

12:15-1:00 **Break-out groups present and discuss over lunch**

1:00-2:45 **Partnerships and Collaboration** – S. Phogat and M. Marovich

- PATH Principles for Private-Sector Collaboration – D. Kaslow
- Malaria Vaccine – D. Kaslow and G. Voss
- Vaccine discovery partnership (VxDP) – F. Randazzo
- Innovative Medicines Initiative (IMI-2); and EU private-public partnership – A. Martini
- Merck/Wellcome, Hilleman Lab – M. Feinberg, Merck
- Small biotech – R. McNally
- TB Drug Accelerator – C. Wilson

2:45-3:15 **Break**

3:15-4:30 **Alignment/Ways Forward** – B. Snow and P. Gomez

- Use the “end to end” perspective to define roles and contributions
- Current collaborations
- Consider alternative models and approaches for HIV vaccine R&D
- Make recommendations and consider follow up actions

4:30-6:00 **Reception**

Appendix B: Meeting Participants

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HIV Vaccine Industry Think Tank: Meeting Summary

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